

**REMARKS**

Claims 74-92 are pending and under examination. Applicants have hereinabove amended claims 74, 75, 79, 81 and 86. Applicants have also canceled claims 91 and 92 without disclaimer or prejudice to applicants' right to pursue the subject matter of these claims in the future. Support for the amendments to claim 74 can be found in Figure 12, and in the specification as originally filed at, *inter alia*, page 32, lines 7 to 23; and at page 48 lines 26-29. The remaining amendments to the claims are merely to introduce minor formatting changes. Accordingly, applicants maintain that this Amendment raises no issue of new matter, and respectfully request entry of this Amendment. After entry of this Amendment, claims 74-90 will be pending and under examination. In view of the amendments made herein and the remarks below, applicants respectfully request that the Examiner's objections and rejections be withdrawn.

**Rejection of Claims Under 35 U.S.C. §112 (Written Description)**

The Examiner rejected claims 74-92 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

Specifically, the Examiner alleged that support for the February 23, 2005 amendment to claim 74 was only provided insofar that the support for passing fluid through the claimed channel existed for a "glass capillary" wherein the channels are in a "chip."

In response, applicants respectfully traverse the Examiner's rejection. However, in order to expedite prosecution, and without

conceding the correctness of the Examiner's argument, applicants have hereinabove amended claim 74 to recite the characteristics identified by the Examiner as having support. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this rejection. Applicants further address below certain remarks by the Examiner.

The Examiner stated that the claimed method has been interpreted as encompassing, *inter alia*, "...simultaneous determination of the masses of an infinite number of DNA fragments, irrespective of the template(s) they were derived from.."

With regard to this, applicants note that the claimed method is directed to sequencing a DNA based on the determination of the masses of a finite number of DNA fragments.

The Examiner also stated that the claimed method has been interpreted as encompassing the use of a plurality of wells connected via a channel, where the channels and wells are within a chip (Emphasis added by applicants).

As applicants have previously observed, no such limitation is recited in the claims. Moreover, the Examiner may not read such limitations into the claims.

The Examiner further alleged that "the device described lacks any means for applying pressure such that any one, much less 96 different samples, could be passed through the coated channels in one direction, much less back-and-forth, thereby permitting/enabling the binding of the DNA sequencing fragments. The Examiner also states that, in reference to page 48 of the

disclosure, "the means for processing the fluid would have each end of a channel in a single well, or the end of a channel could be connected to a plurality of wells. While pressure is to drive the fluid out of the well, through the channel, and into one or more wells, no means other than a perpetual motion could cause this feat to occur."

In response, applicants respectfully note that the specification clearly explains that the phrase "each end of a channel is connected to a single well" as used in page 48 is exemplified in reference to Figure 12 on page 48 ("in the example shown"), which shows that each end of the channel is indeed connected to a single well, but not the same single well as the Examiner appears to have interpreted the specification to indicate. Applicants maintain that one skilled in the art reading the specification and reviewing the example referred to, and explicitly shown, could see that applicant was clearly in possession of the claimed invention. In order to expedite prosecution, however, and without conceding the correctness of the Examiner's position, applicants have hereinabove amended claim 74 to more particularly point out that which applicants consider to be their invention.

The Examiner also asserted that a means for moving a sample through the channel was not adequately described, and that applicants' suggestion that moving fluid through channels is a fundamental technique known to those skilled in the art was conclusory argument. Applicants specifically note that their position, set forth previously, is supported by evidence of the standard use of such means (e.g. a syringe pump) to move fluids through a channel for DNA sequencing on page (iii) of Pang and Yeung, 2000 (Exhibit A of applicants' amendment filed February

23, 2005).

In addition, applicants maintain that one skilled in the art of molecular biology/DNA sequencing (which skill is high) would know such a fundamental technique. Applicants further observe that "information which is well known in the art need not be described in detail in the specification" and that "Generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement" (see MPEP 2163(II)(A)(2), last paragraph).

The Examiner also stated that the claims only require but a single passage of the sample through the channel. In response, applicants note that multiple passages increase the efficiency of the system, but do not constitute a prerequisite for function. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have hereinabove amended claim 74 to more particularly point out that which applicants consider to be their invention.

The Examiner also stated that the claimed method does not recite any step where alkaline salts have been removed from the sample prior to processing.

In response, and without conceding the correctness of the Examiner's position, applicants note that amended claim 74 recites that the surface (to which the DNA fragments have previously attached as set forth in step (e) of claim 74) that is washed in order to remove non-bound components (which necessarily encompasses the alkaline and alkaline-earth salts referred to by

the Examiner) is the surface of the channel recited in step (e).

Applicants again note that the specification also specifically states that the claimed method, because of a purification step where all non-bound components (i.e components of the sample other than DNA sequencing fragments terminated with a biotinylated dideoxynucleotide) are washed away (see page 37 and page 41, lines 9-11), eliminates this problem. Accordingly, the specification itself specifically raises the alkaline salt problem and describes how it is eliminated, and the step to achieve this is recited in the claims.

The Examiner also stated that the claimed method fairly encompasses the use of mass spectrometry in the analysis of the DNA fragments, but that the use of lasers in performing mass spectrometry is recognized in the art as causing significant problems in sequencing.

In response, applicants respectfully traverse the Examiner's position. Initially, applicants note that the mass resolution of the claimed method is sufficient to distinguish the different fragments by mass spectrometry (see figure 2, and page 38, lines 27 to 31). The working examples distinguishing different fragments using MALDI-TOF as described in the specification show that the claimed method is sufficient to distinguish the fragments. Applicants further note that the written description requirement does not require the mechanism of action of how prior art problems are overcome, but merely requires adequate description/possession of the claimed invention. Applicants' claimed invention has been demonstrated by working example as cited above. Accordingly, applicants respectfully request that

the Examiner reconsider and withdraw this ground of rejection.

In view of the above, applicants maintain that the claimed invention satisfies the written description requirement, and respectfully request that the Examiner reconsider and withdraw this rejection.

**Rejection of Claims Under 35 U.S.C. §112 (Enablement)**

The Examiner rejected claims 74-92 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner stated that, as presented above, the specification has not been found to provide an adequate written description of the invention to where the specification does not reasonably suggest that applicant did not possess the entire invention at the time of filing, and that it is well settled that one cannot enable that which they do not yet possess. The Examiner also stated that the record shows that the claimed method fairly encompasses embodiments where art-recognized issues of enablement would be encountered, yet the specification is effectively silent as to how they are to be overcome without the skilled artisan resorting to undue experimentation.

In response, applicants respectfully traverse the Examiner's rejection. Applicants first note that the standards for satisfying the written description and enablement requirements are distinct, and that the ability of one skilled in the art to practice the claimed invention without undue experimentation is the focus of the enablement requirement. Nevertheless, applicants have hereinabove pointed out how the claimed invention is fully described in the specification. Since the Examiner appears to

have based the enablement rejection on an alleged lack of written description, applicants maintain that the enablement requirement is satisfied since, inter alia, the written description requirement is satisfied.

In addition, and as previously noted, in response to the Examiner's statement regarding "art-recognized issues of enablement", applicants maintain that the claimed method is demonstrated in the working examples provided, where DNA is sequenced using MALDI-TOF mass spectrometry. Applicants note that any problems with the different methods discussed in prior art cited by the Examiner as hypothetically applying to the claimed method are not borne out by the empirical results actually obtained using the claimed method and set forth in the specification (as described above). Accordingly, in light of the fact that the claimed invention has been shown to work, hypothetical problems suggested by the Examiner are not germane to the issue of enablement.

Accordingly, applicants maintain that the claimed invention is enabled by the specification, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

#### **Summary**

Applicants maintain that the claims pending are in condition for allowance, and accordingly, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number

Applicant: Jingyue Ju et al.  
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provided below.

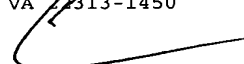
No fee is deemed necessary in connection with the filing of this Amendment. If any fee is required, however, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



John P. White  
Registration No. 28,678  
Alan J. Morrison  
Registration No. 37,399  
Attorneys for Applicants  
Cooper & Dunham LLP  
1185 Ave of the Americas  
New York, New York 10036  
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

  
Alan J. Morrison  
Reg. No. 37,399

- 9/26/01  
Date